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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,322	02/14/2002	David T. Curiel	D6392	8688

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EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	10/075,322	CURIEL ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 24 May 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a inal rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee ave been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 7 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any arned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☒ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1,3-7 and 9-12*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____

10. ☐ Other: _____

DAVID GUZO
PRIMARY EXAMINER

Continuation of 2. NOTE: The proposed claim 7 does not have the same scope as the finally rejected claim 7 due to the amendment of the the preamble of the claim from "A method of gene delivery by adenoviral vector" to "A method of increasing targeting specificity to target cells and reducing transgene expression in non-target cells by adenoviral vector". This amendment would require further consideration and/or search.

Continuation of 5. does NOT place the application in condition for allowance because: Applicants' arguments are respectfully found to be unpersuasive for the rejections of record.

1. With respect to the enablement rejection on the finally rejected claims, Applicants argue basically that the present invention is directed towards improving gene therapy and does not make claims towards obtaining therapeutic effects in vivo. However, one with skill will be able to apply the teachings of this invention in order to obtain therapeutic effects in vivo. Applicants' argument is not persuasive because the sole purpose of a gene therapy is to obtain therapeutic effects, and the instant specification is not enabled to obtain any therapeutic effects via gene therapy upon analysis of the Wands factors already set forth in the final rejection, let alone for improving any gene therapy. Furthermore, as previously pointed out the instant disclosure does not teach any other uses for the gene delivery method other than to attain therapeutic effects. The attainment of any therapeutic effects via gene therapy was and continues to be unpredictable. With the lack of sufficient guidance provided by the present application, it would have required undue experimentation for a skilled artisan to make and use a method of gene delivery by adenoviral vector as claimed.

2. With resepct to the 35 U.S.C. 103 Rejection, Applicants argue mainly that Sosnowski et al. and Muzykantov et al. do not teach or suggest all the elements of the present invention, nor do they provide an incentive or motivation to produce the claimed invention with a reasonable expectation of success. Applicants' arguments are not persuasive because Sosnowski et al. clearly teach a tropism-modified adenoviral vector system using bi-specific antibodies that recognizes an Ad knob protein (specifically 1D6.14 antibody or its Fab fragment) and the target cell-specific receptor to ablate endogenous adenoviral tropism. Sosnowski et al. also teach specifically that any antibody that recognizes a molecule internalized following binding, including but not limited to antibodies to molecules on endothelial cells such as antibodies to FGF receptors, VEGF receptors, E and P-selectins and others. Muzykantov et al. already teach that Mab 9B9 to angiotensin converting enzyme is a safe and specific carrier for drug targeting to the pulmonary endothelium, and that it is internalized by endothelial cells both in vitro and in vivo without significant intracellular degradation. It would have been obvious and an ordinary skilled artisan would have been motivated to modify the tropism-modified adenoviral vector system of Sosnowki et al. by utilizing a bi-specific antibody conjugate linking 1D6.14 and 9B9 antibody to target the modified adenoviral vector specifically to cells of the pulmonary endothelium, and particularly Mab 9B9 has been taught to be a safe and specific carrier for drug targeting to the pumonary endothelium. One of ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Sosnowski et al. and Muzyknatov et al., and a high level of skill of an ordinary skilled artisan.